agent hereby states that the CRF corresponds exactly to the Paper Copy of the Sequence Listing provided herewith. Applicants' agent further hereby states that the contents of the Paper Copy of the Sequence Listing and CRF do not go beyond the disclosure in the Application as filed and do not introduce new matter. A statement by the consultant who prepared the Sequence Listing is additionally provided.

## REMARKS

Applicants respectfully request that the subject application be preliminarily amended as provided in the foregoing amendment. The amendment is made to comply with the Sequence Rules and does not introduce new matter.

However, if for any reason a fee is required, a fee paid is inadequate or credit is owed for any excess fee paid, you are hereby authorized and requested to charge Deposit Account No. **04-1105**.

Respectfully submitted,

Date: July 17, 2002

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**Marked-Up Sections of Specification Showing Changes Made**

**At page 8, please delete lines 7-10, and insert therefore:**

Figs. 1A and 1B shows the nucleic acid (SEQ ID NOS:1 and 3) and amino acid (SEQ ID NOS:2 and 4) sequences of light chain and heavy chain variable regions of H36.D2.B7 with hypervariable regions (CDRs or Complementarity Determining Regions) underlined (single underline for nucleic acid sequences and double underline for amino acid sequences)(SEQ ID NOS. 5-10, respectively, in order of appeareance).

**At page 9, please delete lines 20-27, and insert therefore:**

Figs. 12A-D are drawings showing sequences of partially and fully humanized light chain (LC) variable regions. Figure 12A sequences correspond to SEQ ID NOS. 72-82, respectively, in order of appearance. Light chain CDR sequences CDR sequences of cH36 are shown in Figs. 12B-D (fragment of SEQ ID NO: 2, SEQ ID NO: 6 and SEQ ID NO: 7, respectively). Sequence named "LC-09" is representative of a fully humanized LC framework region.

Figs. 13A-D are sequences of partially and fully humanized heavy chain (LC) variable regions. Figure 13A sequences correspond to SEQ ID NOS 83-96, respectively, in order of appearance. Heavy chain CDR sequences for cH36 and HC-08 are shown in Figs. 13B-D (SEQ ID NO. 8, SEQ ID NOS. 9 and 101 and SEQ ID NO 10, respectively, in order of appearance). Sequence named "HC-08" (SEQ ID NO: 91) is fully humanized HC framework region.

**At page 10, please delete lines 1-5, and insert therefore:**

Figs. 14A-B (SEQ ID NOS. 97 and 98, respectively, in order of appearance) are drawings showing humanized IgG one anti-tissue factor antibody (hOAT (IgG1) constant regions.

Figs. 15A-B (SEQ ID NOS. 99 and 100, respectively, in order of appearance) are drawings showing humanized IgG four anti-tissue factor antibody (hFAT) (IgG4) constant regions.

**At pages 27-28, please delete the section from line 18 on page 27 through line 3 on page 28 and insert therefore:**

More specific humanized antibodies of the invention are those in each of frameworks (FRs) 1, 2, 3 and 4 has at least about 90% amino acid sequence identity, preferably at least about 95% or greater identity to the light chain FR sequences shown in Figure 12A (SEQ ID NOS. 72-82, respectively, in order of appearance). Preferably, the sequence is as shown as "LC-09" (SEQ ID NO. 79) in Figure 12A. Further preferred are those humanized antibodies that include a light chain constant region having at least about 90% amino acid sequence identity, and preferably, at least about 95% sequence identity or greater to the sequence shown in Figure 14A or 15A (SEQ ID NOS. 97 and 99, respectively).

Further specific humanized antibodies are those in which each of frameworks (FRs) 1, 2, 3 and 4 has at least about 90% amino acid sequence identity, preferably about 95% identity or greater to the heavy chain sequences shown in Figure 13A (SEQ ID NOS. 83-96, respectively, in order of appearance). Preferably, the sequence shown as "HC-08" (SEQ ID NO. 91) in Figure 13A. Additional humanized antibodies have a heavy chain constant region with at least about 90% amino acid sequence identity, preferably at least about 95% identity or greater, to sequence shown in Figure 14B or 15B (SEQ ID NOS. 98 and 100, respectively).

**At pages 28-29, please delete the section from line 25 on page 28, through line 16 on page 31, and insert therefore**:

In a more particular embodiment, the first CDR (CDR1) of the heavy chain hypervariable region is at least 90% identical to the CDR1 amino acid sequences shown in Figure 13B (both

SEQ ID NO: 8), preferably at least about 95% identical or greater to that sequence. Typically, the second CDR (CDR2) of the heavy chain hypervariable region is at least 90% identical to the CDR2 amino acid sequence shown in Figure 13C (SEQ ID NOS. 9 and 101, respectively), preferably at least about 95% identical or greater. Preferably also, the third CDR (CDR3) of the heavy chain hypervariable region is at least 90% identical to the CDR3 sequence shown in Figure 13D (both SEQ ID NO: 10), more preferably about 95% identical or greater to that sequence.

In another invention embodiment, the first CDR (CDR1) of the light chain hypervariable region is at least 90% identical to the CDR1 amino acid sequence shown in Figure 12B (fragment of SEQ ID NO: 2), preferably at least about 95% identical or greater. Typically, the second CDR (CDR2) of the light chain hypervariable region is at least 90% identical to the CDR2 amino acid sequence shown in Figure 12C (SEQ ID NO[:]. 6), preferably about 95% identical or greater. Preferably, the third CDR (CDR3) of the light chain hypervariable region is at least 90% identical to the CDR3 amino acid sequence shown in Figure 12D (SEQ ID NO[:]. 7), more preferably about 95% identical or greater to that sequence.

Additional humanized antibodies of the invention include a first framework (FR1) of the heavy chain hypervariable region which FR1 is at least 90% identical to the FR1 amino acid sequence shown in Figure 13A (fragment of SEQ ID NO. 91) as "FR1 HC-08", preferably about 95% identical or greater to that sequence. In one embodiment, the FR1 comprises at least one of the following amino acid changes: E1 to Q; Q5 to V; P9 to G; L11 to V; V12 to K; Q19 to R; and T24 to A. Preferably, the FR1 includes two, three, four, five, or six of those changes with all of those amino acid changes being preferred for many applications.

Further humanized antibodies of the invention include a second framework (FR2) of the heavy chain hypervariable region which FR2 is at least 90% identical to the FR2 sequence shown in Figure 13A (fragment of SEQ ID NO[:]. 91) as "FR2 HC-08", preferably about 95%

identical or greater to that sequence. In one embodiment, the FR2 at least one of the following amino acid changes: 41H to P; and 44S to G. A preferred FR2 includes both of those amino acid changes.

The invention also features humanized antibodies in which a third framework (FR3) of the heavy chain hypervariable region is at least 90% identical to the FR3 sequence shown in Figure 13A (fragment of SEQ ID NO[No]. 91) as "FR3 HC-08", preferably about 95% identical or greater to that sequence. In one embodiment, the FR3 includes at least one of the following amino acid changes: 76S to T; 77T to S; 80F to Y; 82H to E; 84N to S; 87T to R; 89D to E; and 91S to T. A preferred FR3 includes two, three, four, five or six of those amino acid changes with all seven of those amino acid changes being generally preferred.

Also featured are humanized antibodies in which the fourth framework (FR4) of the heavy chain hypervariable region is at least 90% identical to the FR4 amino acid sequence shown in Figure 13A (fragment of SEQ ID NO. 91) as "FR4 HC-08", preferably at least about 95% identical or greater to that sequence. Preferably, the FR4 includes the following amino acid change: 113L to V.

Additional humanized antibodies in accord with the invention feature a first framework (FR1) of the light chain hypervariable region which is at least about 90% identical to the FR1 amino acid sequence shown in Figure 12A (fragment of SEQ ID NO. 79) as "FR1 LC-09", preferably at least about 95% identical or greater to that sequence. In one embodiment, the FR1 comprises at least one of the following amino acid changes: 11Q to L; 15L to V; 17E to D; and 18 to R. A preferred FR1 includes two or three of such amino acid changes with all four amino acid changes being generally preferred.

The present invention also features humanized antibodies in which a second framework (FR2) of the light chain hypervariable region is at least about 90% identical to the FR2 amino acid sequence shown in Figure 12A (fragment of SEQ ID NO. 79) as "FR2 LC-09", preferably at least about 95% identical or greater to that sequence. A preferred FR2 has the following amino acid change: 37Q to L.

Also encompassed by the invention are humanized antibodies in which a third framework (FR3) of the light chain hypervariable region is at least about 90% identical to the FR3 amino acid sequence shown in Figure 12A (fragment of SEQ ID NO. 79) as "FR3 LC-09", preferably at least about 95% identical or greater to that sequence. In one embodiment, the FR3 has at least one of the following amino acid changes: 70K to D, 74K to T, 80A to P, 84A to V, and 85N to T. Preferably, the FR3 has two, three, or four of such amino acid changes with all five of the changes being generally preferred.

Additional humanized antibodies of the invention include a fourth framework (FR4) of the light chain hypervariable region which FR4 is at least about 90% identical to the FR4 sequence shown in Figure 12A (fragment of SEQ ID NO. 79) as "FR4 LC-09", preferably at least about 95% identical or greater to that sequence. In one embodiment, the FR4 includes at least one and preferably all of the following amino acid changes: 100A to Q; and 106L to I.

**At pages 31-34, please delete the section from line 27 on page 31 through page 34, line 11, and insert therefore:**

a) a first CDR (CDR1) which is at least 95% identical to CDR1 amino acid sequences shown in Figure 13B (SEQ ID NO. 8),

b) a second CDR (CDR2) which is at least 95% identical to the CDR2 amino acid sequence shown in Figure 13C (SEQ ID NOS. 9 or 101),

c) a third CDR (CDR3) which is at least 95% identical to the CDR3 amino acid sequence shown in Figure 13D (SEQ ID NO. 10),

d) a first framework (FR1) which is at least 95% identical to the FR1 amino acid sequence shown in Figure 13A (fragment of SEQ ID NO. 91)as "FR1 HC-08" ,

e) a second framework (FR2) which is at least 95% identical to the FR2 amino acid sequence shown in Figure 13A (fragment of SEQ ID NO. 91) as "FR2 HC-08",

f) a third framework (FR3) which is at least 95% identical to the FR3 amino acid sequence shown in Figure 13A (fragment of SEQ ID NO. 91) as "FR3 HC-08", and

g) a fourth framework (FR4) which is at least 95% identical to the FR4 amino acid sequence shown in Figure 13A (fragment of SEQ ID NO[No]. 91) as "FR4 HC-08".

In a particular embodiment, the humanized antibody also includes, on the light chain, at least one of and preferably all of the following components:

h) a first CDR (CDR1) which is at least 95% identical to CDR1 amino acid sequence shown in Figure 12B (fragment of SEQ ID NO.2),

i) a second CDR (CDR2) which is at least 95% identical to the CDR2 amino acid sequence shown in Figure 12C (SEQ ID NO. 6),

j) a third CDR (CDR3) which is at least 95% identical to the CDR3 amino acid sequence shown in Figure 12C (SEQ ID NO. 6),

k) a first framework (FR1) which is at least 95% identical to the FR1 amino acid sequence shown in Figure 12A (fragment of SEQ ID NOS 79) as "FR1 LC-09",

l) a second framework (FR2) which is at least 95% identical to the FR2 amino acid sequence shown in Figure 12A (fragment of SEQ ID NO. 79) as "FR2 LC-09",

m) a third framework (FR3) which is at least 95% identical to the FR3 amino acid sequence shown in Figure 12A (fragment of SEQ ID NO. 79) as "FR3 LC-09", and

n) a fourth framework (FR4) which is at least 95% identical to the FR4 amino acid sequence shown in Figure 12A (fragment of SEQ ID NO[No]. 79) as "FR4 LC-09". Preferably, the humanized antibody further includes the light chain constant sequence of Figure 14A (SEQ ID NO. [No.] 97) or Figure 15A (SEQ ID NO[No]. 99). Also preferably, the antibody includes the heavy chain constant region of Figure 14B (SEQ ID NO[No]. 98) or Figure 15B (SEQ ID NO [No]. 100).

The invention also features a humanized antibody that includes, on the heavy chain, at least one of and preferably all of the following components:

a) a first CDR (CDR1) identical to the CDR1 amino acid sequence shown in Figure 13B (SEQ ID NO. 8),

b) a second CDR (CDR2) identical to the CDR2 amino acid sequence shown in Figure 13C (SEQ ID NOS. 9 or101),

c) a third CDR (CDR3) identical to the CDR3 amino acid sequence shown in Figure 13D (SEQ ID NO. 10),

d) a first framework (FR1) identical to the FR1 amino acid sequence shown in Figure 13A (fragment of SEQ ID NO. 91) as "FR1 HC-08",

e) a second framework (FR2) identical to the FR2 amino acid sequence shown in Figure 13A (fragment of SEQ ID NO. 91) as "FR2 HC-08",

f) a third framework (FR3) identical to the FR3 amino acid sequence shown in Figure 13A (fragment of SEQ ID NO.91) as "FR3 HC-08"; and

g) a fourth framework (FR4) identical to the FR4 amino acid sequence shown in Figure 13A (fragment of SEQ ID NO[No]. 91) as "FR4 HC-08".

In one embodiment, the humanized antibody further includes, on the light chain, at least one of and preferably all of the following components:

h) a first CDR (CDR1) identical to CDR1 amino acid sequence shown in Figure 12B (fragment of SEQ ID NO. 2),

i) a second CDR (CDR2) identical to the CDR2 amino acid sequence shown in Figure 12C (SEQ ID NO. 6),

j) a third CDR (CDR3) identical to the CDR3 amino acid sequence shown in Figure 12D (SEQ ID NO. 7),

k) a first framework (FR1) identical to the FR1 amino acid sequence shown in Figure 12A (fragment of SEQ ID NO. 79) as "FR1 LC-09",

l) a second framework (FR2) identical to the FR2 amino acid sequence shown in Figure 12A (fragment of SEQ ID NO. 79) as "FR2 LC-09",

m) a third framework (FR3) identical to the FR3 amino acid sequence shown in Figure 12A (fragment of SEQ ID NO. 79) as "FR3 LC-09", and

n) a fourth framework (FR4) identical to the FR4 amino acid sequence shown in Figure 12A (fragment of SEQ ID NO[No]. 79) as "FR4 LC-09". Preferably, the humanized antibody further includes the light chain constant sequence of Figure 14A (SEQ ID NO[No]. 97) or Figure 15A (SEQ ID NO[No]. 99). Also preferably, the antibody includes the heavy chain constant region of Figure 14B (SEQ ID NO[No]. 98) or Figure 15B (SEQ ID NO[No]. 100).

**At pages 49- 52, please delete the section from line 24 on page 49 through line 8 on page 52, and insert therefore:**

a) a first CDR (CDR1) which is at least 95% identical to CDR1 amino acid sequence shown in Figure 13B (SEQ ID NO. 8),

b) a second CDR (CDR2) which is at least 95% identical to the CDR2 amino acid sequence shown in Figure 13C (SEQ ID NOS. 9 or 101),

c) a third CDR (CDR3) which is at least 95% identical to the CDR3 amino acid sequence shown in Figure 13D (SEQ ID NO. 10),

d) a first framework (FR1) which is at least 95% identical to the FR1 amino acid sequence shown in Figure 13A (fragment of SEQ ID NO. 91) as "FR1 HC-08",

e) a second framework (FR2) which is at least 95% identical to the FR2 amino acid sequence shown in Figure 13A (fragment of SEQ ID NO. 91) as "FR2 HC-08",

f) a third framework (FR3) which is at least 95% identical to the FR3 amino acid sequence shown in Figure 13A (fragment of SEQ ID NO. 91) as "FR3 HC-08",

g) a fourth framework (FR4) which is at least 95% identical to the FR4 amino acid sequence shown in Figure 13A (fragment of SEQ ID NO[No]. 91) as "FR4 HC-08".

In a more specific invention embodiment, the humanized antibody includes, on the light chain, at least one of, and preferably all of the following components:

h) a first CDR (CDR1) which is at least 95% identical to CDR1 amino acid sequence shown in Figure 12B (fragment of SEQ ID NO. 2),

i) a second CDR (CDR2) which is at least 95% identical to the CDR2 amino acid sequence shown in Figure 12C (SEQ ID NO. 6),

j) a third CDR (CDR3) which is at least 95% identical to the CDR3 amino acid sequence shown in Figure 12D (SEQ ID NO. 7),

k) a first framework (FR1) which is at least 95% identical to the FR1 amino acid sequence shown in Figure 12A (fragment of SEQ ID NO. 79) as "FR1 LC-09",

l) a second framework (FR2) which is at least 95% identical to the FR2 amino acid sequence shown in Figure 12A (fragment of SEQ ID NO. 79) as "FR2 LC-09",

m) a third framework (FR3) which is at least 95% identical to the FR3 amino acid sequence shown in Figure 12A (fragment of SEQ ID NO. 79) as "FR3 LC-09",

n) a fourth framework (FR4) which is at least 95% identical to the FR4 amino acid sequence shown in Figure 12A (fragment of SEQ ID NO[No]. 79) as "FR4 LC-09",

o) a light chain constant region which is at least 95% identical to the amino acid sequence shown in Figure 14A (SEQ ID NO[No]. 97) or Figure 15A (SEQ ID NO[No]. 99); and

p) a heavy chain constant region which is at least 95% identical to the amino acid sequence shown in Figure 14B (SEQ ID NO[No]. 98) or Figure 15B (SEQ ID NO[No]. 100).

In a more specific embodiment of the foregoing method, the humanized antibody or fragment thereof includes, on the heavy chain, at least one of and preferably all of the following components:

a) a first CDR (CDR1) identical to CDR1 amino acid sequence shown in Figure 13B (SEQ ID NO. 8),

b) a second CDR (CDR2) identical to the CDR2 amino acid sequence shown in Figure 13C (SEQ ID NOS. 9 or 101),

c) a third CDR (CDR3) identical to the CDR3 amino acid sequence shown in Figure 13D (SEQ ID NO. 10),

d) a first framework (FR1) identical to the FR1 amino acid sequence shown in Figure 13A (fragment of SEQ ID NO. 91) as "FR1 HC-08",

e) a second framework (FR2) identical to the FR2 amino acid sequence shown in Figure 13A (fragment of SEQ ID NO. 91) as "FR2 HC-08",

f) a third framework (FR3) identical to the FR3 amino acid sequence shown in Figure 13A (fragment of SEQ ID NO. 91) as "FR3 HC-08",

g) a fourth framework (FR4) identical to the FR4 amino acid sequence shown in Figure 13A (fragment of SEQ ID NO[No]. 91) as "FR HC-08";

and on the light chain:

h) a first CDR (CDR1) identical to CDR1 amino acid sequence shown in Figure 12B (fragment of SEQ ID NO. 2),

i) a second CDR (CDR2) identical to the CDR2 amino acid sequence shown in Figure 12C (SEQ ID NO. 6),

j) a third CDR (CDR3) identical to the CDR3 amino acid sequence shown in Figure 12D (SEQ ID NO. 7),

k) a first framework (FR1) identical to the FR1 amino acid sequence shown in Figure 12A (fragment of SEQ ID NO. 79) as "FR1 LC-09",

l) a second framework (FR2) identical to the FR2 amino acid sequence shown in Figure 12A (fragment of SEQ ID NO. 79) as "FR2 LC-09",

m) a third framework (FR3) identical to the FR3 amino acid sequence shown in Figure 12A (fragment of SEQ ID NO. 79) as "FR3 LC-09",

n) a fourth framework (FR4) identical to the FR4 amino acid sequence shown in Figure 12A (fragment of SEQ ID NO[No]. 79) as "FR4 LC-09",

o) a light chain constant region which is identical to the amino acid sequence shown in Figure 14A (SEQ ID NO[No]. 97) or Figure 15A (SEQ ID NO[No]. 99), and

p) a heavy chain constant region which is identical to the amino acid sequence shown in Figure 14B (SEQ ID NO[No]. 98) or Figure 15B (SEQ ID NO[No]. 100).

**At page 65, in Table 1, row 1, please delete the sequence and insert therefore:**

**D**IQMTQSPASQSASLGESV**T**ITC **W**YQQKPGKSPQLL**I**Y cH36-LC (SEQ ID NO: 102)

**At page 65, in Table 1, row 2, please delete the sequence and insert therefore:**

DIQMTQSPASLSASVGDRVTITC WYLQKPGKSPQLLIY Human LC (SEQ ID NO: 27)

**At page 65, in Table 1B, please delete the sequence in row 1, and insert therefore:**

**G**VPSRFSGSGSGT**K**FSFKISSLQ**A**EDFVN**Y**YC **F**GAGTKLEL**K** cH36-LC (fragment of SEQ ID NO: 72)

**At page 65, in Table 1B, please delete the sequence in row 2, and insert therefore:**

GVPSRFSGSGSGTDFSFTISSLQPEDFATYYC FGQGTKLEIK Human-LC (SEQ ID NO: 28)

**At page 66, in Table 2A, please delete the sequence in row 1 and insert therefore:**

EIQLQQSGPELVKPGASVQVSCKTSGYSFT WVRQSHGKSLEWIG cH36-HC (fragment of SEQ ID NO: 83)

**At page 66, in Table 2A, please delete the sequence in row 2, and insert therefore:**

QIQLVQSGGEVKKPGASVRVSCKASGYSFT WVRQSPGKGLEWIG Human-HC (SEQ ID NO: 29)

**At page 66, in Table 2B, please delete the sequence in row 1, and insert therefore:**

KATLTVDKSSTTAFMHLNSLTSDDSAVYFCAR WGQGTTLTVSS cH36-HC (fragment of SEQ ID NO: 83)

**At page 66, in Table 2B, please delete the sequence in row 2, and insert therefore:**

KATLTVDKSTSTAYMELSSLRSEDTAVYFCAR WGQGTTVTVSS Human-HC (SEQ ID NO: 30)

**At pages 69-71, please delete from line 26 on page 61, through line 14 on page 71, and insert therefore:**

Primers Used for Heavy Chain Humanization

TFHC1s2

5' TTTCGTACGTCTTGTCCCAGATCCAGCTGCAGCAGTC 3' (SEQ ID NO. 31)

TFHC1as2

5' AGCGAATTCTGAGGAGACTGTGACAGTGGTGCCTTGGCCCCAG 3'(SEQ ID NO. 32)

TFHC7s

5' GTGAGGCAGAGCCCTGGAAAGGGCCTTGAGTGGATTGG 3'(SEQ ID NO. 33)

TFHC7as

5' CCAATCCACTCAAGGCCCTTTCCAGGGCTCTGCCTCAC 3'(SEQ ID NO. 34)

TFHC5s

5'GCATCTCAACAGCCTGAGATCTGAAGACACTGCAGTTTATTTCTGTG 3'(SEQ ID NO. 35)

TFHC5as2

5' CTGCAGTGTCTTCAGATCTCAGGCTGTTGAGATGCATGAAGGC 3'(SEQ ID NO. 36)

TFHC3as

5' GTCTTCAGATCTCAGGCTGCTGAGCTCCATGAAGGCTGTGGTG 3'(SEQ ID NO. 37)

TFHC2s

5' TACGACTCACTATAGGGCGAATTGG 3'(SEQ ID NO. 38)

TFHC6s

5' CTGTTGACAAGTCTACCAGCACAGCCTACATGGAGCTCAGCAG 3'(SEQ ID NO. 39)

TFHC6as

5' CTGCTGAGCTCCATGTAGGCTGTGCTGGTAGACTTGTCAACAG 3'(SEQ ID NO. 40)

TFHC2as2

5' GCACTGAAGCCCCAGGCTTCACCAGCTCACCTCCAGACTGCTGCAGC 3'(SEQ ID NO. 41)

TFHC3s2

5'CTGGGGCTTCAGTGCGGGTATCCTGCAAGGCTTCTGGTTACTCATTCAC 3'(SEQ ID NO. 42)

TFHC1s3

5' TCGTACGTCTTGTCCCAGATCCAGCTGGTGCAGTCTGGAGGTGAGC 3'(SEQ ID NO. 43)

TFHC2as3

5' GCACTGAAGCCCCAGGCTTCTTCACCTCACCTCCAGACTGCACC 3'(SEQ ID NO. 44)

TFHC9sL

5' GCAGTCTGGACCTGAGCTGAAGAAGCCTGGGG 3'(SEQ ID NO.: 45)

TFHC9asL

5' CCCCAGGCTTCTTCAGCTCAGGTCCAGACTGC 3'(SEQ ID NO. 46)

TFHC8sP

5' GCTGGTGCAGTCTGGACCTGAGGTGAAGAAGCC 3'(SEQ ID NO. 47)

TFHC8asP

5' GGCTTCTTCACCTCAGGTCCAGACTGCACCAGC3'(SEQ ID NO. 48)

TFHC10sK

5' GCAGTCTGGACCTGAGCTGGTGAAGCCTGGGGCTTC 3'(SEQ ID NO. 49)

TFHC10asK

5' GAAGCCCCAGGCTTCACCAGCTCAGGTCCAGACTGC 3'(SEQ ID NO. 50)

LV-1

5' CAGTCTGGACCTGAGGTGGTGAAGCCTGGG 3'(SEQ ID NO. 51)

LV-2

5' CCCAGGCTTCACCACCTCAGGTCCAGACTG 3'(SEQ ID NO. 52)

**At pages 73-75, please delete from line 20 on page 73 through page 75, line 3, and insert therefore:**

TFLC1as2:

5' TTCGAAAAGTGTACTTACGTTTGATCTCCAGCTTGGTCCCAG 3'(SEQ ID NO. 53)

TFLC1s2.1:

5' ACCGGTGATATCCAGATGACCCAGTCTCC 3'(SEQ ID NO. 54)

TFLC5s:

5' GGTTAGCATGGTATCTGCAGAAACCAGGG 3'(SEQ ID NO. 55)

TFLC5as:

5' CCCTGGTTTCTGCAGATACCATGCTAACC 3'(SEQ ID NO. 56)

TFHC2s:

5' TACGACTCACTATAGGGCGAATTGG 3'(SEQ ID NO. 57)

TFLC2as1:

5' CCACAGATGCAGACAGGGAGGCAGGAGACTG 3'(SEQ ID NO. 58)

TFLC1asR:

5' TTCGAAAAGTGTACTTACGTTTGATCTCCAGCTTGGTACCAGCACCGAACG 3'(SEQ ID NO. 59)

TFLC2s:

5' CCTGTCTGCATCTGTGGGAGATAGGGTCACCATCACATGC 3'(SEQ ID NO. 60)

TFLC4as:

5' GATCTCCAGCTTGGTACCCTGACCGAACGTGAATGG 3'(SEQ ID NO. 61)

TFLC3as:

5' GTAGGCTGCTGATCGTGAAAGAAAAGTCTGTGCCAGATCC 3'(SEQ ID NO. 62)

TFLC3s2:

5' CACGATCAGCAGCCTACAGCCTGAAGATTTTGTAAATTATTACTGTC 3'(SEQ ID NO. 63)

TFLC08sds:

5' GCAGCCTACAGCCTGAAGATTTTGCAACTTATTACTGTCAACAAG 3'(SEQ ID NO. 64)

TFLC08sdsa:

5' CTTGTTGACAGTAATAAGTTGCAAAATCTTCAGGCTGTAGGCTGC 3'(SEQ ID NO. 65)

LC105:

5' CAGCAGCCTACAGCCTGAAGATTTTGCAAATTATTACTGTCAAC 3'(SEQ ID NO. 66)

LC103:

5' GTTGACAGTAATAATTTGCAAAATCTTCAGGCTGTAGGCTGCTG 3'(SEQ ID NO. 67)

LC115:

5' CAGTGGATCTGGCACAAAGTTTTCTTTCACGATCAGCAGC 3'(SEQ ID NO. 68)

LC113:

5' GCTGCTGATCGTGAAAGAAAACTTTGTGCCAGATCCACTG 3'(SEQ ID NO. 69)

LC125a:

5' CTGCAGAAACCAGGGCAATCTCCTCAGCTCCTG 3'(SEQ ID NO. 70)

LC123a:

5' CAGGAGCTGAGGAGATTGCCCTGGTTTCTGCAG 3'(SEQ ID NO. 71)

Figure 14 shows hOAT (humanized cH36-IgG1) constant region sequences of the light (Fig. 14A) (SEQ ID NO. 97) and heavy chain (Fig. 14B) (SEQ ID NO: 98). Figure 15 shows hFAT (humanized cH36-IgG4) constant region sequences of the light (Fig. 15A) (SEQ ID NO: 99) and heavy chain (Fig. 15B) (SEQ ID NO[:]. 100). In each figure, the last amino acid residue of the framework 4 (FR4) variable region is connected to the first amino acid residue of the constant region for hOAT and hFAT.

**Marked-Up Version of Claims Showing Changes Being Made**

21. (Amended) The humanized antibody of claim 17, wherein the first CDR (CDR1) of the heavy chain hypervariable region is at least 95% identical to the CDR1 amino acid sequence shown in Figure 13B (SEQ ID NO. 8).

22. (Amended) The humanized antibody of claim 17, wherein the second CDR (CDR2) of the heavy chain hypervariable region is at least 95% identical to the CDR2 amino acid sequence shown in Figure 13C (SEQ ID NOS. 9 or 101).

23. (Amendment) The humanized antibody of claim 17, wherein the third CDR (CDR3) of the heavy chain hypervariable region is at least 95% identical to the CDR3 amino acid sequence shown in Figure 13D (SEQ ID NO. 10).

24. (Amended) The humanized antibody of claim 17, wherein the first CDR (CDR1) of the light chain hypervariable region is at least 95% identical to the CDRl amino acid sequence shown in Figure 12B (SEQ ID NO. 2).

25. (Amended) The humanized antibody of claim 17, wherein the second CDR (CDR2) of the light chain hypervariable region is at least 95% identical to the CDR2 amino acid sequence shown in Figure 12C (SEQ ID NO. 6).

26. (Amended) The humanized antibody of claim 17, wherein the third CDR (CDR3) of the light chain hypervariable region is at least 95% identical to the CDR3 amino acid sequence shown in Figure 12D (SEQ ID NO. 7).

27. (Amended) The humanized antibody of claim 19, wherein the first framework (FR1) of the heavy chain hypervariable region is at least 95% identical to the FR1 amino acid sequence shown in Figure 13A (SEQ ID NO. 91).

29. (Amended) The humanized antibody of claim 19, wherein the second framework (FR2) of the heavy chain hypervariable region is at least 95% identical to the FR2 amino acid sequence shown in Figure 13A (SEQ ID NO. 91).

31. (Amended) The humanized antibody of claim 19, wherein the third framework (FR3) of the heavy chain hypervariable region is at least 95% identical to the FR3 amino acid sequence shown in Figure 13A (SEQ ID NO. 91).

33. (Amended) The humanized antibody of claim 19, wherein the fourth framework (FR4) of the heavy chain hypervariable region is at least 95% identical to the FR4 amino acid sequence shown in Figure 13A (SEQ ID No. 91).

35. (Amended) The humanized antibody of claim 19, wherein the first framework (FR1) of the light chain hypervariable region is at least about 95% identical to the FR1 amino acid sequence shown in Figure 12A (SEQ ID NO. 79).

37. (Amended) The humanized antibody of claim 19, wherein the second framework (FR2) of the light chain hypervariable region is at least about 95% identical to the FR2 amino acid sequence shown in Figure 12A (SEQ ID NO. 79).

39. (Amended) The humanized antibody of claim 19, wherein the third framework (FR3) of the light chain hypervariable region is at least about 95% identical to the FR3 amino acid sequence shown in Figure 12A (SEQ ID NO. 79).

41. (Amended) The humanized antibody of claim 40, wherein the fourth framework (FR4) of the light chain hypervariable region is at least about 95% identical to the FR4 amino acid sequence shown in Figure 12A (SEQ ID NO. 79).

45. (Amended) A humanized antibody comprising at least one murine complementarity determining region (CDR), wherein the antibody binds specifically to human tissue factor (TF) to form a complex, and further wherein factor X or factor IX binding to TF or TF:FVIIa and activation by TF:FVIIa thereto is inhibited, the antibody comprising on the heavy chain:

a) a first CDR (CDR1) which is at least 95% identical to CDR1 amino acid sequence shown in Figure 13B (SEQ ID NO. 8),

b) a second CDR (CDR2) which is at least 95% identical to the CDR2 amino acid sequence shown in Figure 13C (SEQ ID NOS. 9 or 101),

c) a third CDR (CDR3) which is at least 95% identical to the CDR3 amino acid sequence shown in Figure 13D (SEQ ID NO. 10),

d) a first framework (FR1) which is at least 95% identical to the FR1 amino acid sequence shown in Figure 12A (SEQ ID NO. 79),

e) a second framework (FR2) which is at least 95% identical to the FR2 amino acid sequence shown in Figure 12A (SEQ ID NO. 79),

f) a third framework (FR3) which is at least 95% identical to the FR3 amino acid sequence shown in Figure 12A (SEQ ID NO. 79), and

g) a fourth framework (FR4) which is at least 95% identical to the FR4 amino acid sequence shown in Figure 12A (SEQ ID No. 79).

46. (Amended) The antibody of claim 45 further comprising on the light chain,

h) a first CDR (CDR1) which is at least 95% identical to CDR1 amino acid sequence shown in Figure 12B (SEQ ID NO. 2),

i) a second CDR (CDR2) which is at least 95% identical to the CDR2 amino acid sequence shown in Figure 12C (SEQ ID NO. 6),

j) a third CDR (CDR3) which is at least 95% identical to the CDR3 amino acid sequence shown in Figure 12C (SEQ ID NO. 6),

k) a first framework (FR1) which is at least 95% identical to the FR1 amino acid sequence shown in Figure 12A (SEQ ID NO. 79),

l) a second framework (FR2) which is at least 95% identical to the FR2 amino acid sequence shown in Figure 12A (SEQ ID NO. 79),

m) a third framework (FR3) which is at least 95% identical to the FR3 amino acid sequence shown in Figure 12A (SEQ ID NO. 79), and

n) a fourth framework (FR4) which is at least 95% identical to the FR4 amino acid sequence shown in Figure 12A (SEQ ID NO[No]. 79).

47. (Amended) The antibody of claim 45 further comprising the light chain constant sequence of Figure 14A (SEQ ID NO[No]. 97) or Figure 15A (SEQ ID NO[No]. 99).

48. (Amended) The antibody of claim 45 further comprising the heavy chain constant region of Figure 14B (SEQ ID NO[No]. 98) or Figure 15B (SEQ ID NO[No].100).

51. (Amended) A humanized antibody comprising on the heavy chain:

a) a first CDR (CDR1) identical to the CDR1 amino acid sequence shown in Figure 13B (SEQ ID NO. 8),

b) a second CDR (CDR2) identical to the CDR2 amino acid sequence shown in Figure 13C (SEQ ID NOS. 9 or 101),

c) a third CDR (CDR3) identical to the CDR3 amino acid sequence shown in Figure 13D (SEQ ID NO. 10),

d) a first framework (FR1) identical to the FR1 amino acid sequence shown in Figure 13A (SEQ ID NO. 91),

e) a second framework (FR2) identical to the FR2 amino acid sequence shown in Figure 13A (SEQ ID NO. 91),

f) a third framework (FR3) identical to the FR3 amino acid sequence shown in Figure 13A (SEQ ID NO. 91); and

g) a fourth framework (FR4) identical to the FR4 amino acid sequence shown in Figure 13A (SEQ ID No. 91); and

on the light chain:

h) a first CDR (CDR1) identical to CDRl amino acid sequence shown in Figure 12B (SEQ ID NO. 2),

i) a second CDR (CDR2) identical to the CDR2 amino acid sequence shown in Figure 12C (SEQ ID NO. 6),

j) a third CDR (CDR3) identical to the CDR3 amino acid sequence shown in Figure 12D (SEQ ID NO. 7),

k) a first framework (FR1) identical to the FR1 amino acid sequence shown in Figure 12A (SEQ ID NO. 79),

1) a second framework (FR2) identical to the FR2 amino acid sequence shown in Figure 12A (SEQ ID NO. 79),

m) a third framework (FR3) identical to the FR3 amino acid sequence shown in Figure 12A (SEQ ID NO. 79), and

n) a fourth framework (FR4) identical to the FR4 amino acid sequence shown in Figure 12A (SEQ ID NO[No]. 79).

52. (Amended) The antibody of claim 51 further comprising the light chain constant sequence of Figure 14A (SEQ ID NO[No]. 97) or Figure 15A (SEQ ID NO[No]. 99).

53. (Amended) The antibody of claim 51 further comprising the heavy chain constant sequence of Figure 14B (SEQ ID NO[No]. 98) or 15B (SEQ ID NO[No].100).

65. (Amended) A method of inhibiting blood coagulation in a mammal, the method comprising administering to the mammal, an effective amount of a humanized antibody or fragment thereof wherein the antibody binds specifically to human tissue factor (TF) to form a complex, and further wherein factor X or factor IX binding to TF or TF:FVIIa and activation by TF:FVIIa thereto is inhibited, the antibody or fragment comprising on the heavy chain:

a) a first CDR (CDRl) which is at least 95% identical to CDR1 amino acid sequence shown in Figure 13B (SEQ ID NO. 8),

b) a second CDR (CDR2) which is at least 95% identical to the CDR2 amino acid sequence shown in Figure 13C (SEQ ID NOS. 9 or 101),

c) a third CDR (CDR3) which is at least 95% identical to the CDR3 amino acid sequence shown in Figure 13D (SEQ ID NO. 10),

d) a first framework (FR1) which is at least 95% identical to the FR1 amino acid sequence shown in Figure 13A (SEQ ID NO. 91),

e) a second framework (FR2) which is at least 95% identical to the FR2 amino acid sequence shown in Figure 13A (SEQ ID NO. 91),

f) a third framework (FR3) which is at least 95% identical to the FR3 amino acid sequence shown in Figure 13A (SEQ ID NO. 91),

g) a fourth framework (FR4) which is at least 95% identical to the FR4 amino acid sequence shown in Figure 13A (SEQ ID NO[No]. 91);

and on the light chain,

h) a first CDR (CDR1) which is at least 95% identical to CDR1 amino acid sequence shown in Figure 12B (SEQ ID NO. 2),

i) a second CDR (CDR2) which is at least 95% identical to the CDR2 amino acid sequence shown in Figure 12C (SEQ ID NO. 6),

j) a third CDR (CDR3) which is at least 95% identical to the CDR3 amino acid sequence shown in Figure 12D (SEQ ID NO. 7),

k) a first framework (FR1) which is at least 95% identical to the FR1 amino acid sequence shown in Figure 12A (SEQ ID NO. 79),

1) a second framework (FR2) which is at least 95% identical to the FR2 amino acid sequence shown in Figure 12A (SEQ ID NO. 79),

m) a third framework (FR3) which is at least 95% identical to the FR3 amino acid sequence shown in Figure 12A (SEQ ID NO. 79),

n) a fourth framework (FR4) which is at least 95% identical to the FR4 amino acid sequence shown in Figure 12A (SEQ ID NO[No]. 79),

o) a light chain constant region which is at least 95% identical to the amino acid sequence shown in Figure 14A (SEQ ID NO[No]. 97) or Figure 15A (SEQ ID NO[No]. 99), and

p) a heavy chain constant region which is at least 95% identical to the amino acid sequence shown in Figure 14B (SEQ ID NO[No]. 98) or Figure 15B (SEQ ID NO[No].100).

66. (Amended) A method of inhibiting blood coagulation in a mammal, the method comprising administering to the mammal, an effective amount of a humanized antibody or fragment thereof wherein the antibody binds specifically to human tissue factor (TF) to form a complex, and further wherein factor X or factor IX binding to TF or TF:FVIIa and activation by TF:FVIIa thereto is inhibited, the antibody or fragment comprising on the heavy chain:

a) a first CDR (CDR1) identical to CDR1 amino acid sequence shown in Figure 13B (SEQ ID NO. 8),

b) a second CDR (CDR2) identical to the CDR2 amino acid sequence shown in Figure 13C (SEQ ID NOS. 9 or 101),

c) a third CDR (CDR3) identical to the CDR3 amino acid sequence shown in Figure 13D (SEQ ID NO. 10),

d) a first framework (FR1) identical to the FR1 amino acid sequence shown in Figure 13A (SEQ ID NO. 91),

e) a second framework (FR2) identical to the FR2 amino acid sequence shown in Figure 13A (SEQ ID NO. 91),

f) a third framework (FR3) identical to the FR3 amino acid sequence shown in Figure 13A (SEQ ID NO. 91),

g) a fourth framework (FR4) identical to the FR4 amino acid sequence shown in Figure 13A (SEQ ID No. 91);

and on the light chain:

h) a first CDR (CDR1) identical to CDR1 amino acid sequence shown in Figure 12B (SEQ ID NO. 2),

i) a second CDR (CDR2) identical to the CDR2 amino acid sequence shown in Figure 12C (SEQ ID NO. 6),

j) a third CDR (CDR3) identical to the CDR3 amino acid sequence shown in Figure 12D (SEQ ID NO. 7),

k) a first framework (FR1) identical to the FR1 amino acid sequence shown in Figure 12A (SEQ ID NO. 79),

1) a second framework (FR2) identical to the FR2 amino acid sequence shown in Figure 12A (SEQ ID NO. 79),

m) a third framework (FR3) identical to the FR3 amino acid sequence shown in Figure 12A (SEQ ID NO. 79),

n) a fourth framework (FR4) identical to the FR4 amino acid sequence shown in Figure 12A (SEQ ID No. 79),

o) a light chain constant region which is identical to the amino acid sequence shown in Figure 14A (SEQ ID NO[No]. 97) or Figure 15A (SEQ ID NO[No]. 99), and

p) a heavy chain constant region which is identical to the amino acid sequence shown in Figure 14B (SEQ ID NO[No]. 98) or Figure 15B (SEQ ID NO[No]. 100).